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-1696                                                          TGTTTGCATTAAGTTC
-1680 ATAGATTATAATTTGTAATGGAATCAACACCAAATGCAAATTAGAAAGAGAGCCCACTTTGCTCACCCAGTCACGTCTTC
-1600 CCATGTAACCATAGAACGTTGGGGTCCTGTGTCTTTCTAGATCCACAGTCTTGCTCTCAGAACAGGCTAGCCACACCACA
-1520 GGCCTAGTGCCAGGACCCATGGCCTTTTTTTTAAGCTCAGACTCCCTTCTGTGAACAGCAATATCCCCACAACTTGTACAA
-1440 CATTGGTGCTTCCTGCAAGGGCTACAGAACTATTTGATACGAAAATGTTCATTGACTTACACACAAGAAGCACAAAAT
-1360 AAAAAATTAATAATTAATTTAATGTCTTTGAAAATGTACCATTTATTTTTACATTTGGGGTCATAAGAATTGTATTACAC
-1280 TTAAGAATGCAATACAATTTGAAGATCAGATTTTTCTCCCTTTGTGAGAATTTCTCAGTATGTGTGATGACTACCAAGAA
-1200 ATCATAGCCAGTCATAAATTCAGTGAGTTACTCATAAACGAACAAGAACCACCTACTTCTTGGGGAGGTAGGTCTGCTTC
-1120 CCTTCAACTCAGGATACAACTGCTTTCAACTGCTTTCTTCACATTAGCTGACTAATTAGCTAGAAGCCTGTCGTAAACAA
-1040 TTTTATGGTTGACTCCTTCCCTGGGCTCAGGGTTCCCTAGAACAGAGAGGTCCCCAAATCCCGGTCTGTGGCCTGTCCGC
 -960 CTAAGCTCTGCCTCCTGCCAGATCAGCAGGCAGCATTAGATTCTCATAGGAGCTGGACGCCTATTGTGAACTGCGCATGT
 -880 GCGGGATCCAGATTGTGCACTCTTTATGAGAATCTAACTAATGCTTGATGATCTATCTGAACCAGAACAATTTCATCCTG
 -800 AAACCATCCCCCACCAATCCATAGAAATACTGTCTTCCACAAAAATGATCCCTGGTGCCAAAAATGTTAGAGACCACTCC
 -720 CCTAAAACTCTCTTCTTAGCTCTCACCTCCTGTATTACTATCTCATCTCAGTACATTGAAGCCCCCATCTTTTCCCCATG
 -640 GATGCCTCATTTCCTATTAGGGAGGCATTTTTTTATTTTTTGTTTTTATTTTTTTCCGAGACGGAGTCTCGCTCTGTCGC
 -560 CAAGGCTGGAGTGCAGTGGCGCGATCTCGGCTCACTGCAAGCTCCGCCTCCCGGGTTCACGCCATTCTCCTGCCTCAGCC
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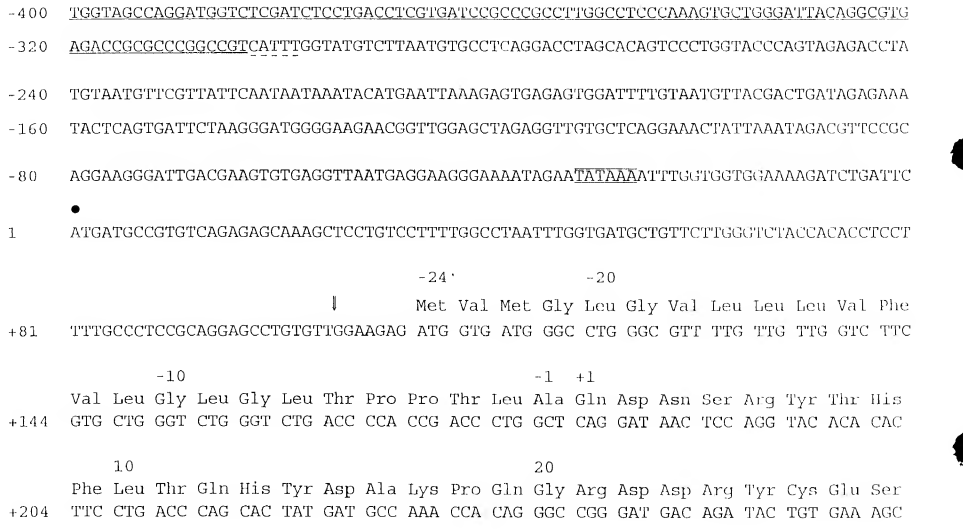
Fig. 1A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-160 TACTCAGTGATTCTAAGGGATGGGGAAGAACGGTTGGAGCTAGAGGTTGTGCTCAGGAAACTATTAAATAGACGTTCCGC
-80 AGGAAGGGATTGACGAAGTGTGAGGTTAATGAGGAAGGGAAAATAGAATATAAAATTTGGTGGTGGAAAAGATCTGATTC
1 ATGATGCCGTGTCAGAGAGCAAAGCTCCTGTCCTTTTGGCCTAATTTGGTGATGCTGTTCTTGGGTCTACCACACCTCCT
-24 -20
Met Val Met Gly Leu Gly Val Leu Leu Leu Val Phe
+81 TTTGCCCTCCGCAGGAGCCTGTGTTGGAAGAG ATG GTG ATG GGC CTG GGC GTT TTG TTG TTG GTC TTC
-10 -1 +1
Val Leu Gly Leu Gly Leu Thr Pro Pro Thr Leu Ala Gln Asp Asn Ser Arg Tyr Thr His
+144 GTG CTG GGT CTG GGT CTG ACC CCA CCG ACC CTG GCT CAG GAT AAC TCC AGG TAC ACA CAC
10 20
Phe Leu Thr Gln His Tyr Asp Ala Lys Pro Gln Gly Arg Asp Asp Arg Tyr Cys Glu Ser
+204 TTC CTG ACC CAG CAC TAT GAT GCC AAA CCA CAG GGC CGG GAT GAC AGA TAC TGT GAA AGC

Fig. 1B

```
                                         40
     30
     Ile Met Arg Arg Arg Gly Leu Thr Ser Pro Cys Lys Asp Ile Asn Thr Phe Ile His Gly
+264 ATC ATG AGG AGA CGG GGC CTG ACC TCA CCC TGC AAA GAC ATC AAC ACA TTT ATT CAT GGC

                                         60
     50
     Asn Lys Arg Ser Ile Lys Ala Ile Cys Glu Asn Lys Asn Gly Asn Pro His Arg Glu Asn
+324 AAC AAG CGC AGC ATC AAG GCC ATC TGT GAA AAC AAG AAT GGA AAC CCT CAC AGA GAA AAC

                                         80
     70
     Leu Arg Ile Ser Lys Ser Ser Phe Gln Val Thr Thr Cys Lys Leu His Gly Gly Ser Pro
+384 CTA AGA ATA AGC AAG TCT TCT TTC CAG GTC ACC ACT TGC AAG CTA CAT GGA GGT TCC CCC

                                         100
     90
     Trp Pro Pro Cys Gln Tyr Arg Ala Thr Ala Gly Phe Arg Asn Val Val Val Ala Cys Glu
+444 TGG CCT CCA TGC CAG TAC CGA GCC ACA GCG GGG TTC AGA AAC GTT GTT GTT GCT TGT GAA

                                         120         123
     110
     Asn Gly Leu Pro Val His Leu Asp Gln Ser Ile Phe Arg Arg Pro Stop
+504 AAT GGC TTA CCT GTC CAC TTG GAT CAG TCA ATT TTC CGT CGT CCG TAA

+552 CCAGCGGGCCCCTGGTCAAGTGCTGGCTCTGCTGTCCTTGCCTTCCATTTCCCCTCTGCA
+612 CCCAGAACAGTGGTGGCAACATTCATTGCCAAGGGCCCAAAGAAAGAGCTACCTGGACCTTTTGTTTTCTGTTTGACAAC
                                                    ⇓
+692 ATGTTTAATAAATAAAAATGTCTTGATATCAGTAAGAATCAGAGTCTTCTCACTGATTCTGGCATATTGATCTTTCCCC
+782 CATTTTCTCTACTTGGCTGCTCCCTGAGAGGACTGCATAGGATAGAAATGCCTTTTTCTTTTCTTTTCGTTTTTTTTTTT
```

Fig. 1C

+862 TTTTTTTTTTGAGATGGAGTCTCACTCTGTCGCCCAGGCTTAAGTGCAATGGCACAATCTCGGCTCACTGCAACCTCTCT

+942 CTCCTGGGTTCAAGTGATTCTCCTGCCTCAGCCTCCCAAATAGCTGAGATTACAGGCATGCACCACCACACCTGGCTAAT

+1022 TTTTGTGTTTTTAGTAGAGACAGGGTTTCACCGTTTTGGCCAGGTTGGTCTTGAACTCCTGACCTCGGGAGATCCGCCCA

+1102 CCTTGGCCTCTCTTTGTGCTGGGATTACAGGCATGAGCCACTGAGCCGGGCCACTTTTTCCTTATCAGTCAGTTTTTACA

+1182 AGTCATTAGGGAGGTAGACTTTACCTCTCTGTGAAGGAAAGTATGGTATGTTGATCTACAGAGAGAGATGGAAAAATTCC

+1262 AGGGCTCGTAGCTACTAAGCAGAATTTCCAAGATAGGCAAATTGTTTTTTCTGTCAAATAATAAGCTAATATTACTTCTA

+1342 CAAATATGAGACCTTGGAGAGAAGTTTCCAAGGACCAAGTACCAACATACCAACAGATTATTATAGTTTCTCTCACTCTT

+1422 ACACACACACACACACATATACACATATGTAATCCAGCATGAATACCAAAATTCATTCAGGGTAGCCACCTTTTGTCTTA

+1502 ATCGAGAGATAATTTTGATGTTTGAATGGAATGCTCCCAGGATATTCTCTTGTCATGGTTATTTTATATAAAATTCAAAA

+1582 ACCAATTACATTATTTCCTCTGTAATCTTTTACTTTATCAACTAATGTCTGGCAAGTGTGATGTTTTGGGGAAGTTATAG

+1662 AAGATTCCGGCCAGGCGCTTATCTCACGCTTGTAATCCAGCACTTTGGGAAGCTGAGGCCGACAGATCACGAGGTCAAGA

+1742 GATCAAGACCATCCTGGACAACATGGTGAAACCTTGTCTCTACTAAAAATGTGAAAATTAGCTGGGCGTGGTGGCACACA

+1822 CCTATAGTCCCAGCTACTCGGGAGGCTGAGGCAGGAGAATCGCTTGAACCTAGGAGGCGGAGGTTGCACTGAGCCGAGAT

+1902 CACGCCACTGCACTCCAGCCTGGGCGACAGAGCGAGACTCCATCTCAAAAAAAAAAAAAAAAGAAAGATCCCAGTTTATC

+1982 CCAGTTTATCCCTTATTCTTCCTCAATTCTCAAGATTTGTTTTTAAGTTAACATAACTTAGGTTAACACACTCTTTGTAA

+2062 AATACACTGTTCAATCTACAGACTCAGTGGTTAGCTTCCTGTTAACTAATTTCTGTTGACAGGTACTTGGATATTTTATT

Fig. 1D

+2142 TAGAAAGTGGTTGCCAATAAATTAGTTATAAGTCGCCAGTTTCACTGCCTTGTGAACACATAATTATTGTGGTCTCAGTA

+2222 TTCCCTATGGTGGCTTCTCCTGCTCCTGGTATTGCCCTGAAATGGGCCAAAAGCCGTGGCTCCCCAATGCTCAGGTTATA

+2302 GAACATTGTCCAGGTACCACCTAGGAGAGCCCAGCCTCACTGAAAGTATTCAAATTTAGGAATGGGTTTGAGAAGTAGGT

+2382 AGCTGGTATGTGCTTAGCACAAGAATCTCTCTTCCTTGGGTTAGTCTGTTTCAAAACTGAAAACACTGTCATTCCTTAAG

+2462 AAAATAGGAAAAAGTATTCCAAACCTCTGTCACTAGAAAATTTGCCATATTACCAAATCTCAAAAACCTCTCAGGAAATG

+2542 AGAAAGTCCCAGTTTCTGGTAAACTATTTGGGCCCTTTTCTCAAGTTCTCCTTCCAGTGCTATTTCCTTGAGGTGAGGCA

+2622 AAGTTACTCAAGATCATCGCTGCCACTCAAGGCCTTGATAGGGCAAGTGAAAGGCATGGACCATTATTATATTGATCACA

+2702 GCATAAGCTGTGAAAACCCACATCTTCTCCAAACATCTGCTTGGAGCATTATCATCGCATAGTTTGCTCTGGTGTTCAGG

+2782 GAAATCGCTGTTTCATAGGAAATCACATGGCAGTGGGATGGGAGTGTTTCCTGACCTGCCGATGGTACTGGCACCTGAGC

+2862 AAGCATTCCTAGTCCTTTTTGGTCTGGGCCTCTTGTTCTATCACAACCACAAGCTGTTTAAAATAAAAACGTCAAGTCAC

+2942 AGGCAGGTCATTTTATCCTGCGTGAATCAATTGAAG

Fig. 1E

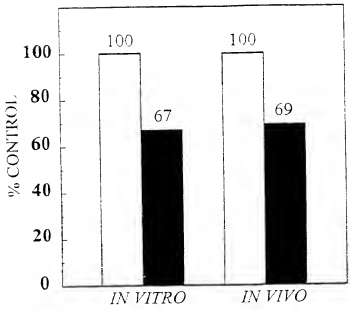

% CONTROL
100
80
60
40
20
0
100
67
100
69
IN VITRO
IN VIVO

Fig. 2A

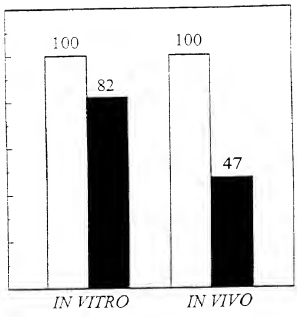

100
82
100
47
IN VITRO
IN VIVO

Fig. 2B

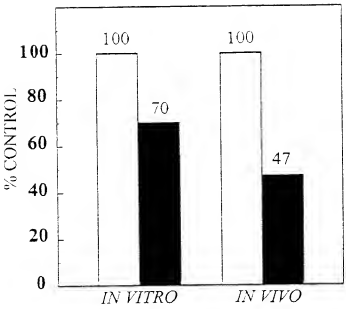

% CONTROL
100
80
60
40
20
0
100
70
100
47
IN VITRO
IN VIVO

Fig. 3A

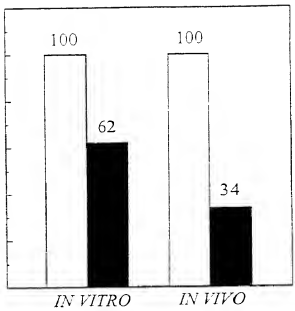
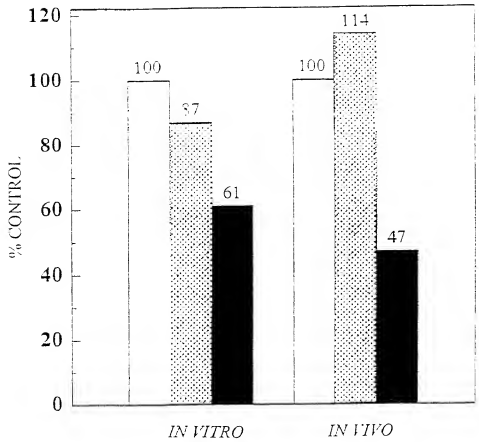

100
62
100
34
IN VITRO
IN VIVO

Fig. 3B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60
40
20
0
% CONTROL
100
87
61
100
114
47
IN VITRO
IN VIVO

Fig. 4

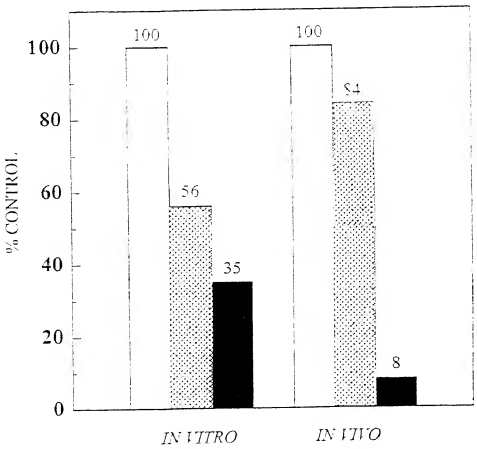

Fig. 5

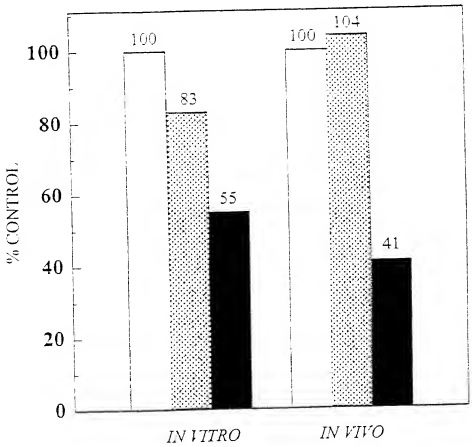

Fig. 6

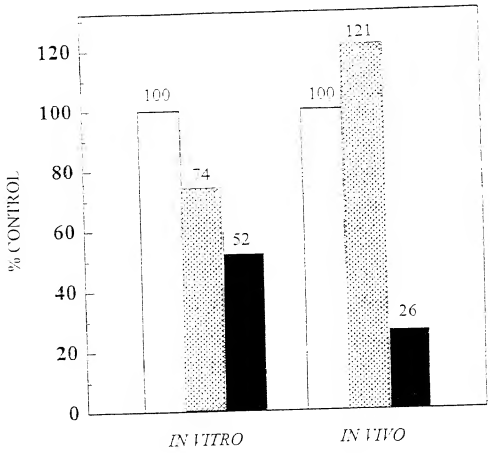
120
100
80
60
40
20
0
% CONTROL
100
74
52
100
121
26
IN VITRO
IN VIVO

Fig. 7

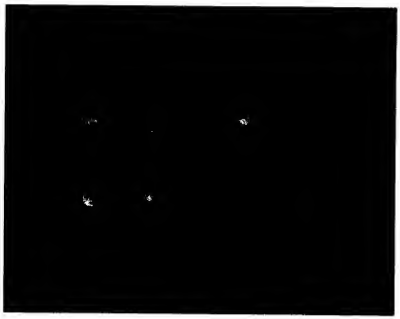

FIG. 8

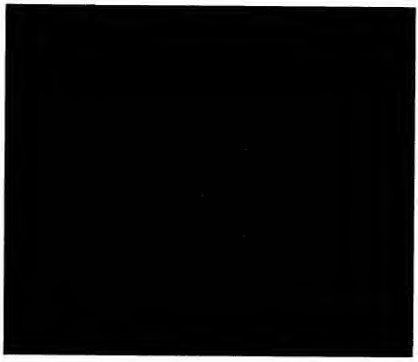

FIG. 9

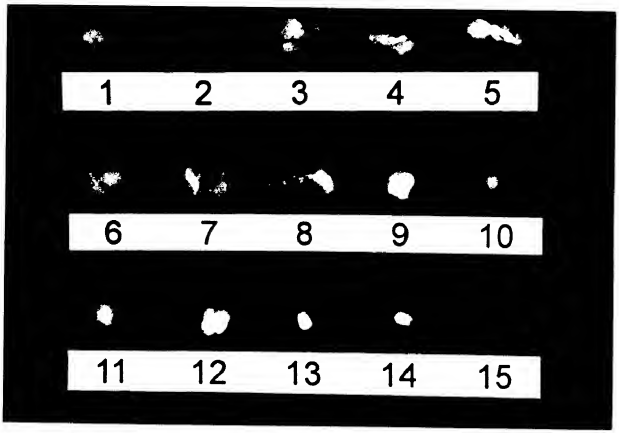

FIG. 10

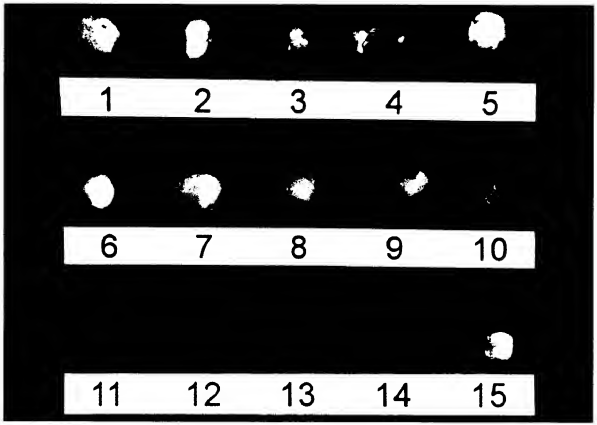

FIG. 11

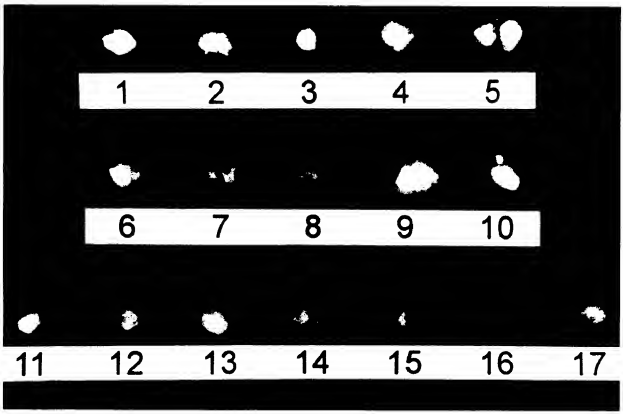

FIG. 12

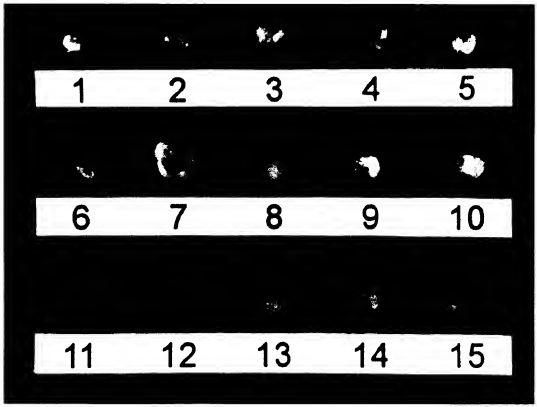

FIG. 13

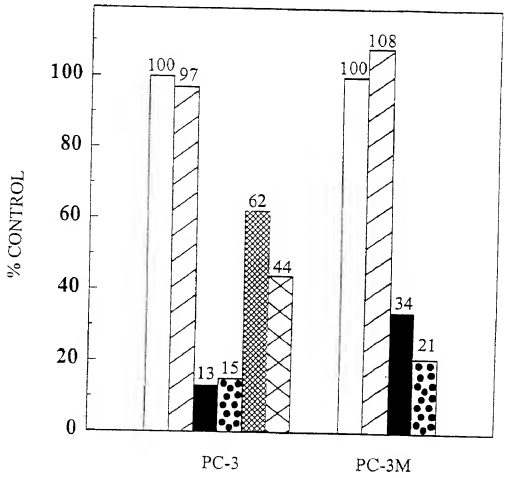

Fig. 14

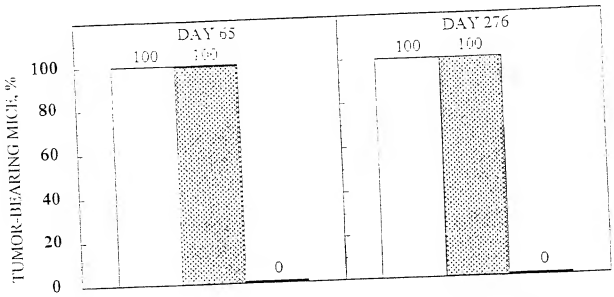

Fig. 15A

Fig. 15B

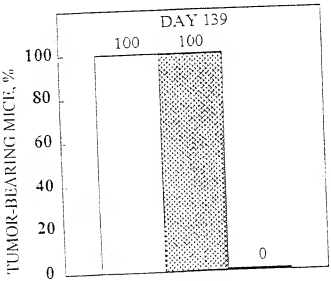

Fig. 15C

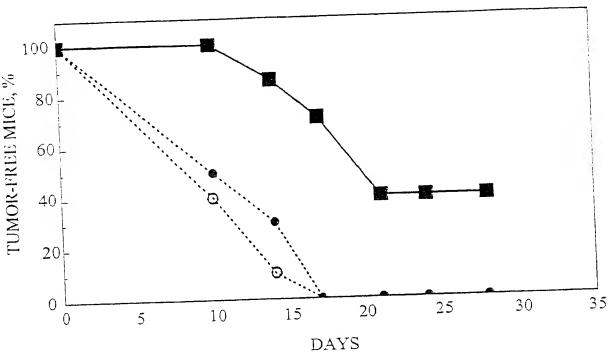

Fig. 16

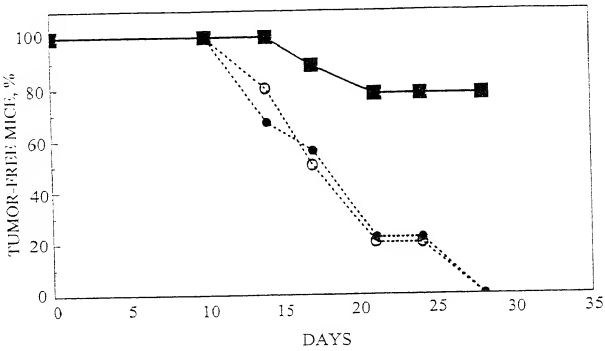

Fig. 17